AMENDMENTS TO THE CLAIMS

Claims:

- 1. (Currently Amended) A recombinant HuEPO-L-vFc fusion protein consisting of comprising HuEPO, a peptide linker, and a human IgG Fc variant, wherein the recombinant HuEPO-L-vFc fusion protein exhibits in vitro biological activity similar to or higher than that of rHuEPO on a molar basis.
- 2. (Currently Amended) The <u>recombinant HuEPO-L-vFc fusion protein of Claim 1</u>, wherein the peptide linker in claim 1 containing about 20 or fewer amino acids is present between HuEPO and the human IgG Fc variant; and the peptide linker comprises two or more amino acids selected from the group consisting of glycine, serine, alanine, and threonine.
- 3. (Currently Amended) The recombinant HuEPO-L-vFc fusion protein of Claim 1 or Claim 2, wherein the human IgG Fc variant in claim 1 or claim 2 comprising comprises a hinge, CH2, and CH3 domains of human IgG2 with Pro331Ser mutation as of SEQ ID NO: 18.
- 4. (Withdrawn) The human IgG Fc variant in claim 1 or claim 2 comprising a hinge, CH2, and CH3 domains of human IgG4 with Ser228Pro and Leu235Ala mutations as SEO ID NO: 20.
- 5. (Withdrawn) The human IgG Fc variant in claim 1 or claim 2 comprising a hinge, CH2, and CH3 domains of human IgG1 with Leu234Val, Leu235Ala, and Pro331Ser mutations as SEQ ID NO: 22.

- 6. (Withdrawn) The HuEPO-L-vFc fusion protein of any of the preceding claims exhibits in vitro biological activity similar to or higher than that of rHuEPO on a molar basis.
- 7. (Currently Amended) A CHO-derived cell line transfected with DNA encoding the recombinant producing the HuEPO-L-vFc fusion protein of any of the preceding claims produces in its growth medium in excess of 10 µg per million cells in a 24 hour period.
- 8. (Original) The CHO-derived cell line producing the HuEPO-L-vFc fusion protein of claim 7 in its growth medium in excess of 30 μg per million cells in a 24 hour period.
- 9. (Currently Amended) The CHO-derived cell line producing the HuEPO-L-vFc fusion protein of claim 1, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG selected from the group consisting of IgG1 as SEQ ID NO: 22, IgG2 as of SEQ ID NO: 18, and IgG4 as SEQ ID NO: 20, and the IgG Fc contains amino acid mutations to attenuate effector functions, a flexible peptide linker containing about 20 or fewer amino acids is present between HuEPO and human IgG Fc variant, and the HuEPO-L vFc fusion protein exhibits in vitro biological activity similar to or higher than that of rHuEPO on a molar basis.
- 10. (Currently Amended) A method for making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant, which wherein said method comprises: (a) generating a CHO-derived cell line; (b) growing the cell line under conditions wherein the recombinant fusion protein is expressed in its growth medium in excess of 10 µg per million cells in a 24 hour period; and (c) purifying the expressed recombinant fusion protein from step (b), wherein the recombinant fusion protein exhibits in vitro biological activity similar to or higher than that of rHuEPO on a molar basis.

- 11. (Currently Amended) The method of claim 10, wherein the flexible peptide linker containing about 20 or fewer amino acids is present between HuEPO and the human IgG Fc variant; and the peptide linker comprises two or more amino acids selected from the group consisting of glycine, serine, alanine, and threonine.
- 12. (Currently Amended) The method of claim 10, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG2 of SEQ ID NO: 18 with Pro331Ser mutation.
- 13. (Withdrawn) The method of claim 10, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG4 with Ser228Pro and Leu235Ala mutations.
- 14. (Withdrawn) The method of claim 10, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG1 with Leu234Val, Leu235Ala, and Pro331Ser mutations as SEQ ID NO: 18.
- 15. (Currently Amended) The method of any claim of claims 10, 11, and 12, 13, and 14, wherein step (b) is in excess of 30 μg per million cells in a 24 hour period.
- 16. (Withdrawn) The method of claim 10, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG4 with Ser228Pro and Leu235Ala mutations as SEQ ID NO: 20.
- 17. (Withdrawn) The method of claim-16, wherein step (b) is in excess of 30 μg per million cells in a 24 hour period.

- 18. (Withdrawn) The method of claim 10, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG1 with Leu234Val, Leu235Ala, and Pro331Ser mutations as SEQ ID NO: 22.
- 19. (Withdrawn) The method of claim 18, wherein step (b) is in excess of 30 μg per million cells in a 24 hour period.
- 20. (Currently Amended) A method for making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant, which method comprises: (a) generating a CHO-derived cell line transfected with DNA encoding the recombinant HuEPO-L-vFC fusion protein; (b) growing the CHO cell line under conditions the recombinant protein is expressed in its growth medium in excess of 10 ug per million cells in a 24 hour period; and (c) purifying the expressed protein from step (b), wherein the recombinant fusion protein exhibits in vitro biological activity similar to or higher than that of rHuEPO on a molar basis; wherein the flexible peptide linker containing about 20 or fewer amino acids is present between HuEPO and the human IgG Fc variant; and the peptide linker comprises two or more amino acids selected from the group consisting of glycine, serine, alanine, and threonine; wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains selected from the group consisting of human IgG2 with Pro331Ser mutation as of SEQ ID NO: 18, human IgG4 with Ser228Pro and Leu235Ala mutations as SEQ ID NO: 20, and human IgG1 with Leu234Val, Leu235Ala, and Pro331Ser mutations as SEQ ID NO: 22.